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| 08/736,267 | 10/24/1996 | KJELL G. E. BACKSTROM | 06275/004001 | 3709 |

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EXAMINER

LUKTON, DAVID

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Please find below and/or attached an Office communication concerning this application or proceeding.

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Please find below a communication from the EXAMINER in charge of this application.

Commissioner of Patents

Please see the attached PTO-892 and the attached communication regarding the amendment filed
4/9/02.

Pursuant to the directives of paper No. 46 (filed 4/9/02), claims 28 and 88 have been cancelled, and claims 1, 2, 21, 29, 30, 56, 59, 78, 89, 90, 93, 94, 96 amended. Claims 1-10, 12-16, 21, 22, 26, 27, 29-32, 50-87, 89-97, 101-118 are pending. Claims 2, 21, 22, 26, 27, 29, 30, 32, 50-87, 89-97 remain withdrawn from consideration.

In the previous Office action, claims 1, 3-10, 12-16, 31, 101, 102, 103-118 characterized as allowable to the extent that they have been examined. What was sought was compliance with the restriction requirement (paper No. 35, mailed 12/30/99). This meant exclusion of "non-hygroscopic additives" from the claims. Instead of excluding such, applicants have substituted the word "excipients" for "additives" in claim 1. However, this amendment is deemed non-responsive. Applicants have argued in effect that the term "excipient" is sufficiently well defined such as to exclude any and all biologically active peptides. Applicants have pointed to a dictionary definition of the term at issue which describes "excipient" as being "more or less inert". However, the term at issue is very much imprecise, and is not effective to exclude any and all biologically active peptides. First, merely because a word can be found in a dictionary does not mean that it is well-defined. Consider, for example, the following words from everyday English: hot, cold, near, far, sharp, dull, large, small, easy, difficult, clear and vague. Where exactly is the dividing line between, for example, "hot" and "cold"...? Second, in the specification,

cyclodextrans have been characterized as "active" agents. Yet cyclodextrans are often used as excipients (this is disclosed in, e.g., the following US patents 6383513, 2002052366, 2002051752, 6380198, 6379717, 2002049200, 6358530, 2001051613, and 6310089).

Thus, are cyclodextrans "active" agents or are they "inert"...? In addition, albumin is sometimes used as an excipient. Is albumin really "inert" to the point that it serves no function in mammals? In addition, there is the issue of the amount of the peptide. Regardless of how active a peptide may be, below a certain dosage, it exhibits no perceptible efficacy. For example, if one had a composition consisting of 0.1% human growth hormone, and 99.9% cellulose, and 100 mg of the composition were administered, would this 100 mg be "active" or "inert"...?

In addition to the foregoing, consider the following references on excipients:

Kalinkova G N (*International Journal of Pharmaceutics* 187 (1) 1-15, 1999)

Pifferi G (*FARMACO* 54 (1-2) 1-14, 1999)

Barbaud A (*Clinical Reviews in Allergy and Immunology* 13 (3) 253-63, 1995)

As is evident, many excipients are far from inert. Perhaps, if there had been a detailed and specific definition of the term "excipients" in the specification such that pharmacologically active peptides were excluded in any and all amounts, then use of the term "excipients" in the claims would be effective to exclude such. But as it happens, the term

is not sufficiently well defined to exclude pharmacologically active peptides in any and all amounts. As such, the amendment to claim 1 does not bring the claims into compliance with the restriction requirement. Moreover, claim 61 does not recite the term "excipient" at all. It remains the case that if part (C) is included, claim 1 would effectively set 10 microns as a lower limit on particle size, rather than an upper limit, and moreover, there would be no lower limit on the amount of 10 micron particles. Thus, claim 1 would encompass compositions in which the particle sizes occupy a range of 10 microns to, e.g., 500 microns, and moreover, would permit the 10 micron particles to be present at only the parts-per-million range. This is a very different invention from that encompassed by claim 1 in which part (C) is excluded. In this latter invention, no less than 50% of the total mass must consist of particles having a diameter of 10 microns or less. In accordance with the foregoing, applicants are held non-responsive. What is again sought was compliance with the restriction requirement (paper No. 35, mailed 12/30/99). This will mean exclusion of "non-hygroscopic excipients" from the claims. (As indicated previously, an exception to the foregoing is made in the case of claim 102 and claims properly subgeneric thereto; although claim 102 contains non-elected subject matter, the restriction will not be enforced in the case of this claim, since the "additives" are limited to specific compounds, or to specific classes of compounds).

Cancellation of the method claims and apparatus claims is not required; however, those

method claims and apparatus claims which are drawn to compositions which are not included within the scope of the elected claims will not be rejoined. For example, claim 56 permits any "bile salt derivative"; this is not permitted by claim 1, and so claim 56 would not be rejoined in its present form. (It is suggested that the method claims and apparatus claims be amended as appropriate in order to "streamline" prosecution).

As indicated above, the amendment filed 4/9/02 is non-responsive. Applicants are required to amend the claims in accordance with the foregoing, or take other action as deemed appropriate. Failure to take such action will result in abandonment of the application. The time for response is reset pursuant to this Office action, and is one month from its mailing.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton [phone number (703)308-3213].

An inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



DAVID LUKTON
PATENT EXAMINER
GROUP 120